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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,700	02/27/2002	Todd W. Seeley	PP-01406.004 / 200130.438	1172

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,700	SEELEY, TODD W.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

od for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

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1)☒ Responsive to communication(s) filed on *31 March 2004*.

a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

position of Claims

4)☒ Claim(s) *4-6 and 16-48* is/are pending in the application.

4a) Of the above claim(s) *5,6,16-41,47 and 48* is/are withdrawn from consideration.

5)☒ Claim(s) *4* is/are allowed.

6)☒ Claim(s) *42-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

plication Papers

9)☐ The specification is objected to by the Examiner.

0)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

1)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

ority under 35 U.S.C. §§ 119 and 120

2)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

3)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

4)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

chment(s)

☐ Notice of References Cited (PTO-892)

☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .

4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 03/31/04 has been acknowledged.

Claims 4, 42-46 are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Election/Restrictions

This application contains claims 5-6, 16-41 and 47-48 drawn to an invention nonelected with traverse in the reply filed on 09/03/03. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

Claims 42-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the same reasons of record as set forth in the office action mailed on 12/02/03.

The scope of invention as claimed encompasses any variant of huBUB3 protein which has 90% identity to a nucleic acid sequence which encodes the amino acid sequences of SEQ ID NO:2. The scope of invention as claimed also encompasses a variant of SEQ ID NO:2 which 95% identical to amino acid sequences of SEQ ID NO:2.

The scope of invention as claimed encompasses an epitope bearing portion of the polypeptide of SEQ ID NO:2, wherein in the epitope comprises about 8-25 contiguous amino acid sequences of SEQ ID NO:2.

At best the specification only disclosed the amino acid sequences of SEQ ID NO:2 (huBUB3). The specification as filed fails to disclose any variant of huBUB3 polypeptide that has huBUB3 like activity explicitly or implicitly as putatively claimed herein. In addition the specification fails to define any epitope-bearing portion found in the polypeptide of SEQ ID NO:2. Similarly the specification fails to define a fusion protein that consists of at least 8 contiguous amino acids huBUB3 protein as shown in SEQ ID NO:2.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case the specification only amino acid sequence of SEQ ID NO:2 which encodes HuBUB3 protein. The specification fails define any variant or epitope-bearing portion of huBUB3 protein. The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In the instant case the polypeptide variants (as claimed) has been defined only by a statement of function that broadly encompasses a huBUB3 like protein activity or an antibody binding portion of huBUB3 protein (epitope), which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. The state of the art at the time

of filing was such that defining epitopes is not as easy as it seems. Even when the epitope is defined in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (see Greenspan et al, Nature Biotechnology 7:936-937, 1999).

Response to arguments

The applicant argues that in the human BUB3 protein as disclosed in the specification can be considered a genus. The applicant argues that the specific examples that support the scope of the claims are BUB3 proteins with one or more conservative amino acid substitution and variants of BUB3 protein. The applicant argues that one cannot say that the specification fails to describe the features of that genus "even in passing," because the specification clearly discloses and describes huBUB3 protein and variants thereof. The applicant argues that the human huBUB3 protein is specifically known to exist and so a situation involving the absence of knowledge as to what material consists of simply is not applicable in the instant case. The applicant argues applicants are their own lexicographer therefore can define an epitopes according to present invention. The applicant further argues that protein folding is a theoretical issue and one skill in the art would be aware of issues related to further experimentation.

However, applicant's arguments are found NOT persuasive because the disclosure of a single species does not represent a genus (see *Written Description Requirement guidelines)*. Besides the amino acid sequences of SEQ ID NO:2 (huBUB3), the specification fails to disclose any other variant of huBUB3 polypeptide that has huBUB3-like activity explicitly or implicitly. In addition the specification fails to define any epitope-bearing portion found on the polypeptide of SEQ ID NO:2. Furthermore the polypeptide variants (as claimed) has been defined only by a statement of function that broadly encompasses a huBUB3-like protein activity or an antibody binding portion of huBUB3 protein (epitope), which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. The possession may be shown by actual reduction

to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention.

The applicant argument that an applicant is his or her own lexicographer (especially when defining an epitope) is considered moot, since the earlier office action clearly provided the evidence that defining epitopes is not as easy as it seems. Even when the epitope is defined in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (see Greenspan et al, Nature Biotechnology 7:936-937, 1999). Therefore according to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim

Claims 42-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a an isolated huBUB3 polypeptide comprising the amino acid sequences of SEQ ID NO:2, does not reasonably provide enablement for any variant or an epitope bearing portion of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, for the same reasons of record as set forth in the office action mailed on 12/02/03.

Nature of Invention:

Invention relates to variants and epitopes of huBUB3 protein.

Breadth of Claims and Guidance Provided in the Specification:

The scope of invention as claimed encompasses any variant of huBUB3 protein which has 90% identity to a nucleic acid sequence which encodes the amino acid sequences of SEQ ID NO:2. the scope of invention as claimed also encompasses a variant of SEQ ID NO:2 which 95% identical to amino acid sequences of SEQ ID NO:2. The scope of invention as claimed encompasses an epitope bearing portion of the

polypeptide of SEQ ID NO:2, wherein in the epitope comprises about 8-25 contiguous amino acid sequences of SEQ ID NO:2. At best the specification only disclosed the amino acid sequences of SEQ ID NO:2 (huBUB3). The specification as filed fails to disclose any variant of huBUB3 polypeptide that has huBUB3 like activity explicitly or implicitly as putatively claimed herein. In addition the specification fails to define any epitope-bearing portion found in the polypeptide of SEQ ID NO:2. Similarly the specification fails to define a fusion protein that consists of at least 8 contiguous amino acids huBUB3 protein as shown in SEQ ID NO:2.

State of Art and Predictability:

The art at the time of filing define epitopes as a region on an antigen molecule to which antibody or the T cell receptor binds specifically. Antibodies binds in a more or less exact three-dimensional fit within an epitope. This structure may be formed from residues on different regions of protein antigen molecules, which in the native state are closely apposed due to protein folding. Thus the 3-dimensional structure of the protein molecule is considered essential. Epitopes recognized by T cells are peptide fragments processed by APCs. Since a continuous primary sequence is necessary for T cell recognition but not for antibody recognition, the epitopes recognized on the same protein molecule by each (antibody or T-cell) are different. In this regard, the specification fails to provide sufficient guidance and objective evidence as to the linear or three-dimensional conformation of the huBUB polypeptide, which may or may not constitute an epitope (see Herbert et al. The Dictionary of Immunology, Academic Press, 4th edition, 1995). Moreover, defining epitopes is not as easy as it seems. Even when the epitope is defined in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (Greenspan et al, Nature Biotechnology 7:936-937 (1999) see page 937, 2 column). Furthermore 5-10% variation (90-95% identical) as claimed would certainly affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Furthermore, mere identification of critical

regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976).

Response to arguments

The applicant argues that to make a prima facie case of lack of enablement, the PTO must come forward with reasons and supported showing why the specification fails to enable one of ordinary skill in the art to make and use the claimed invention. The mere fact that some experimentation is necessary does not negate enablement as long as undue experimentation is not required. The applicant argues that the identification or production of a huBUB3 polypeptide falling within the scope of the present claims may require some experimentation but if viewed in the light of Wands this experimentation, and the possibility of experimentation is not undue. The applicant argues that the present application provides extensive guidance to allow one of ordinary skill in the art to obtain a polypeptide that is within the scope of the claims.

However, applicant's arguments are found NOT persuasive. The earlier office action clearly provided the evidence that screening of any and all natural and non-natural variants of huBUB3 protein, wherein at 5-10% amino acid are added substituted and/or deleted in the amino acid sequences of the SEQ ID NO:2 is not considered routine in the art. Making and testing a point mutation is significantly different from the making and testing an amino acid sequences wherein at least 5-10% amino acids are added, deleted and/or substituted. The scope of invention as claimed is not limited to a single point mutation but encompasses a variation of at least 5-10% in the amino acid sequences of SEQ ID NO:2. The number of possible scenario increase geometrically with increase in percent non-identity (5-10%). Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. In addition one has to engage in extensive making and testing in order to obtain variants or epitopes that meet the

requirements for the huBUB3 function, since defining epitopes is not as easy as it seems (see Greenspan et al, Nature Biotechnology 7:936-937 (1999). This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed, since the applicant has not presented enablement commensurate in scope with the claims.

Conclusion

Claim 4 is allowed.

Claims 42-46 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769 (**571-272-0769**). The examiner can normally be reached on Mon-Fri.

from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel Ph.D. can be reached on 571-272-0781 (**571-272-0781**). The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
Patent examiner

JEFFREY FREDMAN
PRIMARY EXAMINER